IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Patent Application No. 10/586,072

Applicant: Brough

Filed: July 14, 2006

TC/AU: 1632

Examiner: Wu Cheng Winston Shen

Docket No.: 253625

Customer No.: 23460

APPELLANTS' REPLY BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Appellants hereby file a Reply Brief to the Examiner's Answer. The Examiner's Answer was mailed by the U.S. Patent and Trademark Office on April 13, 2011. Thus, this Reply Brief is due June 13, 2011. This Reply Brief is provided in further support of the appeal from the final rejection dated March 24, 2010.

Discussion of Obviousness Rejections

In the Appeal Brief, Appellants argued that (1) the Examiner has failed to make out a *prima facie* case of obviousness by providing any credible reason for one of ordinary skill in the art to have chosen, with a reasonable expectation of success, an Ad28 vector to deliver Hath-1 to change the sensory perception of an animal, and (2) the evidence of record reflects that the claimed invention exhibits unexpected properties, which would rebut a *prima facie* case of obviousness even if properly made out by the Examiner.

In the Examiner's Answer, the Examiner provides only one reason – that Ad28 is a "close species" to the Ad36 viruses disclosed in Wigand et al. – as to why one of ordinary skill in the art would have chosen an Ad28 vector to deliver Hath-1 to change the sensory perception of an animal with a reasonable expectation of success (Examiner's Answer at page 12, lines 5-6). The Examiner bases this conclusion on the notion that one of ordinary skill in

the art allegedly would have considered expressing a gene of interest from adenoviral vectors of different serotypes as "routine optimization," as evidenced by the disclosures of Zoghbi et al. and Falck-Pedersen et al. (Examiner's Answer at page 27, lines 6-9). The Examiner provides no support for such a notion, let alone that one of ordinary skill in the art would have had a reasonable expectation of success of using any particular adenoviral vector, such as an Ad28 vector, to provide Hath1 to generate sensory hair cells that allow perception of stimuli in the inner ear, thereby changing the sensory perception of an animal.

Contrary to the assertions of the Examiner, Appellants have not "selectively ignored" certain disclosures of the cited references (e.g., Falck-Pedersen et al.). Rather, Appellants have pointed out that the disclosures of the cited references do not provide a sufficient basis for concluding that one of ordinary skill would have had a credible reason to use an Ad28 vector to transduce supporting cells of the inner ear with a reasonable expectation of success in generating sensory hair cells that allow perception of stimuli in the inner ear, thereby changing the sensory perception of an animal.

Indeed, Appellants have acknowledged that Falck-Pedersen et al. discloses the construction of non-group C adenoviral vectors of different serotypes, including serotype D (of which serotype 28 is a member). Appellants also have acknowledged that Bout et al. discloses that different adenovirus serotypes exhibit different tropisms. However, the fact remains that these cited references do not disclose that any adenovirus serotypes exhibit tropism for the supporting cells of the inner ear, let alone provide a basis for one of ordinary skill in the art to have used an Ad28 vector to transduce supporting cells of the inner ear with a reasonable expectation of success in generating sensory hair cells that allow perception of stimuli in the inner ear, thereby changing the sensory perception of an animal.

The disclosure that one adenovirus serotype can be used to infect cells of a particular tissue does not mean that a related adenovirus serotype, or even the same adenovirus serotype, can be used to infect cells of a different tissue. For example, Ad36 was known to infect cells of adipose tissue at the time of the present invention, as evidenced by, e.g., Dhurandhar et al., *Int. J. Obes. Relat. Metab. Disord.*, *24*(8): 989-996 (2000), and Dhurandhar et al., *Int. J. Obes. Relat. Metab. Disord.*, *25*(7): 990-996 (2001). Such knowledge would not cause one of ordinary skill in the art to choose Ad36 or any other adenovirus reported to be similar thereto, such as Ad28 as disclosed in Wigand et al., to transduce cells of the inner ear with a reasonable expectation of success in generating sensory

hair cells that allow perception of stimuli in the inner ear, thereby changing the sensory perception of an animal.

The Examiner states that sensory hair cells are not adipose cells and that Wigand et al. does not disclose any disadvantage associated with adenovirus infection of adipose tissue. Again, the fact that one adenovirus serotype can be successfully used to infect cells of a particular tissue, such as adipose tissue, does not mean that a related adenovirus serotype, or even the same adenovirus serotype, can be successfully used to infect cells of a different tissue, such as the supporting cells of the inner ear. The Examiner has cited to nothing in the record which supports the Examiner's position in this respect.

Thus, the Examiner has not articulated a reason with a rational underpinning to explain why one of ordinary skill in the art would have selected an Ad28 vector to transduce supporting cells of the inner ear and deliver a nucleic acid sequence encoding Hath1 with a reasonable expectation of success of providing Hath1 to generate sensory hair cells that allow perception of stimuli in the inner ear, thereby changing the sensory perception of an animal. As a result, the Examiner has failed to make out a *prima facie* case of obviousness with respect to the appealed claims.

Furthermore, even if the Examiner had properly made out a *prima facie* case of obviousness, the evidence of record reflects that the claimed invention exhibits unexpected properties, which would rebut a *prima facie* case of obviousness.

The Rule 132 declarations of Douglas E. Brough filed on February 26, 2009, and December 17, 2009, demonstrate, *inter alia*, that certain non-subgroup C adenoviral vectors, such as an Ad28 vector, unexpectedly exhibit enhanced delivery to sensory cells of the inner ear as compared to a subgroup C adenoviral vector and that this enhanced delivery is not merely the result of the non-subgroup C adenoviral vector not being a subgroup C adenoviral vector. The results described in the Rule 132 declarations were not predictable based on the disclosures of the cited references, whether considered alone or in the aggregate.

The Examiner continues to characterize the results described in the Rule 132 declarations as "exactly as expected" in view of the prior art because non-subgroup C adenoviral vectors were developed to overcome technical difficulties associated with subgroup C adenoviral vectors, such as Ad5 (Office Action dated March 24, 2010, at page 21, third complete paragraph). One of ordinary skill in the art would not have expected that a

non-subgroup C adenoviral vector (e.g., Ad28) would perform the same as, much less better than, a subgroup C adenoviral vector based solely on the fact that non-subgroup C adenoviral vectors were developed as an alternative to subgroup C adenoviral vectors. While one of ordinary skill in the art arguably may have expected a non-subgroup C adenoviral vector to exhibit reduced immunogenicity in a human, neutralization of an adenoviral vector is but one of many factors that contribute to the transduction efficiency of an adenoviral vector.

Appellants maintain that none of Kovesdi et al., Staecker et al., Wickham et al., and Mizuguchi et al. compensates for the deficiencies of Zoghbi et al., Falck Pedersen et al., Bout et al., and Wigand et al. set forth above. In this respect, Kovesdi et al., Staecker et al., Wickham et al., and Mizuguchi et al. do not disclose or suggest a serotype 28 adenoviral vector which comprises a nucleic acid sequence encoding Hath1 operably linked to a promoter that functions in supporting cells of the inner ear, much less a method of using such an adenoviral vector to change the sensory perception of an animal. Moreover, each of Kovesdi et al., Staecker et al., Wickham et al., and Mizuguchi et al. fails to provide a credible reason for one of ordinary skill in the art to utilize a serotype 28 adenoviral vector to deliver a nucleic acid sequence encoding Hath1 to the inner ear, with a reasonable expectation of success, based on the combined disclosures of Zoghbi et al., Falck-Pedersen et al., Bout et al., and Wigand et al. in the manner set forth by the Examiner.

Conclusion

For the reasons set out in Appellants' Brief on Appeal, and as further explained above in view of the Examiner's Answer, Appellants respectfully reiterate that the obviousness rejection under Section 103 should be reversed.

Respectfully submitted,

/Melissa E. Kolom/
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